# Consortium for Blood Group Genes (CBGG): 2009 report

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The Consortium for Blood Group Genes is a worldwide organization whose goal is to have a vehicle to interact, establish guidelines, operate a proficiency program, and provide education for laboratories involved in DNA and RNA testing for the prediction of blood group, platelet, and neutrophil antigens. Currently, the consortium operates with representatives from Brazil, Canada, and the United States. Membership is voluntary with the expectation that members actively contribute to discussions involving blood group genetics. This year witnessed a change in the standing committee membership and the institution of a representative for the human platelet antigens group. Looking forward, the consortium sees challenges for the nomenclature of blood group alleles and user-required specifications for laboratory information systems to store genotype information. ***Immunohematology 2010;26:47–50.***

**Key Words:** blood group alleles, Consortium for Blood Group Genes, proficiency, target alleles

The Consortium for Blood Group Genes (CBGG) is a not-for-profit organization established in 2004 by a group of like-minded people with scientific or industry experience and interest in the field of the genetics of red cell, platelet, and neutrophil antigens, collectively known as blood group genetics. The mission of the consortium is "to establish guidelines, to provide education, and to provide a proficiency exchange for laboratories involved in DNA or RNA testing for the determination of blood group, platelet, and neutrophil antigens." The consortium is coordinated by three country representatives: Lilian Castilho (Hemocentro de Campinas) for Brazil, Maryse St-Louis (Héma-Québec) for Canada, and Connie Westhoff (American Red Cross) for the United States, with Marion Reid (New York Blood Center) as facilitator and Greg Denomme (BloodCenter of Wisconsin) as secretary. Vagner Castro is coordinator for the platelet group. Members are encouraged to refer to the published CBGG articles for background information and progress of the consortium.[1–5] Exchange of information is mainly accomplished through electronic mailings and a yearly meeting, with proficiency evaluation exercises occurring in the spring and fall of each year.

## The CBGG Document

The *CBGG Document* is the sole information document for members, is made available by electronic transfer, and outlines the function of the CBGG. This document contains information on the structure, organizational rules and bylaws, regulatory compliance plan, preferred terminology, and progress on the working parties including a summary of the proficiency exchange program (from 2007 to date), guidelines of practice, DNA repository, funding, forms and disclaimers, and proposed Web site. It is highly recommended that CBGG members refer to this document for the aforementioned duties and activities. A meeting is held annually, in part for members to discuss outstanding issues, to provide input, to accept amendments, and to summarize the proficiency evaluations.

## Regulatory Affairs

CBGG members continue to recognize the importance of appropriately worded reports, including the use of disclaimers, of molecular analyses for both blood donors and transfusion recipients. Data from molecular testing continue to be a source of information for the resolution of complex serologic problems, and presently are not intended as the sole means for patient transfusion management decisions.

As an international consortium, CBGG does not provide guidance on regulatory affairs; members are responsible for knowledge of and compliance with the regulations in their own countries. For US members, we bring to your attention the Code of Federal Regulations (CFR) Part 864—Hematology and Pathology Devices, Subpart E—Specimen Preparation Reagents; Sec. 864.4020 Analyte specific reagents.

## Allele Nomenclature

The list of target alleles was adopted by the CBGG in 2007 and updated in 2009. The preferred current terminology is listed under the heading "Target antigen (target allele)" in Table 1 of this report. However, the final naming of alleles awaits the decision of the International Society for Blood Transfusion. When referring to a particular single nucleotide change, it is important to follow the designated notation, e.g., 125G>A, with intronic nucleotide changes represented in the lower case, e.g., –67t>c. The associated amino acid substitutions flank the designated position number, e.g., Pro103Ser or P103S. Because gene numbering systems vary, and to avoid ambiguity in the location of nucleotide changes, the CBGG has adopted GenBank gene reference sequences (RefSeqGene) and reference SNP numbers (rs#) for blood group genes and nucleotides (Table 1). These numbers refer to a set of common documents used to communicate or report molecular testing results and are linked to other GenBank reference files.

**Table 1.** List of targets and recommended controls for prediction of certain RBC antigens†

| ISBT system name (symbol) number | Target antigen (target allele) | ISBT gene name (RefSeqGene) | Target nucleotide (SNP rs#)‡ | Controls and comments (monitor assay performance with DNA controls known to be homozygous and heterozygote for both alleles unless otherwise noted) |
|---|---|---|---|---|
| ABO (ABO) 001 | A (*ABO*A1*) | *ABO* (NG_006669.1) | consensus | Targets for nondeletional (261ΔG) ABO*O alleles are not listed. Various alleles have been described and multiple targets or sequencing is required for identification. |
| | A2 (*ABO*A2*) | | nt 1061ΔC (rs56392308) | |
| | B (*ABO*B1*) | | nt 526C>G (rs7853989)<br>nt 703G>A (rs8176743)<br>nt 796C>A (rs8176746)<br>nt 803G>C (rs8176747) | |
| | O (*ABO*O1*) | | nt 261G/ΔG (rs8176719) | |
| MNS (MNS) 002 | M (*GYPA*M*)<br>N (*GYPA*N*) | *GYPA* (NG_007470.2) | nt 59C>T;71G>A;72T>G (rs7682260;7687256; 7658293) | Position 72 is the 3rd nt of codon 24 (not for clinical use). |
| | S (*GPB*S*)<br>s (*GPB*s*) | *GYPB* (NG_007483.1) | nt 143T>C (rs7683365) | |
| | S silenced | | nt 230C>T, intron 5+5g>t | 230T/T not required, I5+5t/t not required |
| Rh (RH) 004 | D | *RHD* (NG_007494)<br>*RHDΨ* | Exon 4 and 7<br>Exon 4 37-bp insert | Targets may vary as there are many approaches. |
| | C (*RHCE*C*)<br>c (*RHCE*c*) | *RHCE* (NG_009208) | intron 2 insertion<br>nt 307T>C (rs676785) | |
| | E (*RHCE*E*)<br>e (*RHCE*e*) | | nt 676C>G (rs609320) | |
| | $C^w$ | | nt 122A>G | 122G/G not required |
| | $C^x$ | | nt 106G>A | 106A/A not required |
| | V & VS | | nt 733C>G (rs1053361) | 733G/G not required |
| | V (VS−) | | nt 1006G>T | 1006T/T not required |
| Lutheran (LU) 005 | $Lu^a$ (*LU*01* or *LU*A*)<br>$Lu^b$ (*LU*02* or *LU*B*) | *LU* (NG_007480.1) | nt 230A>G (rs28399653) | |
| Kell (KEL) 006 | K (*KEL*01*)<br>k (*KEL*02*) | *KEL* (NG_007492.1) | nt 578T>C (rs8176058) | |
| | $Kp^a$ (*KEL*03*)<br>$Kp^b$ (*KEL*04*) | | nt 841T>C (rs8176059) | |
| | $Js^a$ (*KEL*06*)<br>$Js^b$ (*KEL*07*) | | nt 1790C>T (rs8176038) | |
| Duffy (FY) 008 | $Fy^a$ (*FY*01* or *FY*A*)<br>$Fy^b$ (*FY*02* or *FY*B*) | *FY* (NG_011626.1) | nt 125G>A (rs12075) | |
| | $Fy^x$ (*FY*265T*) | | nt 265C>T (rs34599082) | 265T/T not required |
| | Fy null (RBC) | | nt -67t>c (rs2814778) | GATA nucleotide change |
| Kidd (JK) 009 | $Jk^a$ (*JK*01* or *JK*A*)<br>$Jk^b$ (*JK*02* or *JK*B*) | JK (NG_011775.1) | nt 838G>A (rs1058396) | Testing for nulls may be appropriate in some situations. |
| Diego (DI) 010 | $Di^a$ (*DI*01* or *DI*A*)<br>$Di^b$ (*DI*02 or DI*B*) | *DI* (NG_007498.1) | nt 2561T>C (rs2285644) | |
| Yt (YT) 011 | $Yt^a$ (*YT*01* or *YT*A*)<br>$Yt^b$ (*YT*02* or *YT*B*) | *YT* (NG_007474.1) | nt 1057C>A (rs1799805) | |
| Scianna (SC) 013 | Sc1 (*SC*01*)<br>Sc2 (*SC*02*) | *SC* (NG_008749.1) | nt 169G>A (rs56025238) | 169A/A not required |
| Dombrock (DO) 014 | $Do^a$ (*DO*01* or *DO*A*)<br>$Do^b$ (*DO*02* or *DO*B*) | *DO* (NG_007477.1) | nt 793A>G (rs11276) | |
| | Hy (*HY*) | | nt 323G>T (rs28362797) | |
| | $Jo^a$ (*JO*) | | nt 350C>T (rs28362798) | |
| Colton (CO) 015 | $Co^a$ (*CO*01* or *CO*A*)<br>$Co^b$ (*CO*02* or *CO*B*) | *CO* (NG_007475.1) | nt 134C>T (rs28362692) | 134T/T not required |
| Landsteiner-Wiener (LW) 016 | $LW^a$ (*LW*05* or *LW*A*)<br>$LW^b$ (*LW*07* or *LW*B*) | *LW* (NG_007728.1) | nt 308A>G | 308G/G not required |
| Cromer (CR) 021 | $Cr^a$ (*CR*01* or *CR*A*) | *CROM* (NG_007465.1) | nt 679G>C (rs60822373) | |
| Knops (KN) 022 | $Kn^a$ (*KN*01* or *KN*A*)<br>$Kn^b$ (*KN*02* or *KN*B*) | *KN* (NG_007481.1) | nt 4681G>A (rs41274768) | |
| | $McC^a$ (*KN*03*)<br>$McC^b$ (*KN*06*) | | nt 4768A>G (rs17047660) | 4768G/G not required |
| | $Sl^a$ (*KN*04*)<br>Vil (*KN*07*) | | nt 4801A>G (rs17047661) | 4801G/G not required |
| Indian (IN) 023 | $In^a$ (*IN*01* or *IN*A*)<br>$In^b$ (*IN*02* or *IN*B*) | *IN* (NG_008937.1) | nt 252C>G | |
| OK (OK) 024 | $Ok^a$ (*OK*01* or *OK*A*) | *OK* (NG_007468.1) | nt 274G>A | Homozygous mutated and heterozygote not required |

†Predicted antigen negativity should be confirmed by hemagglutination with licensed reagents if available, with unlicensed reagents if available, or by a crossmatch performed by the laboratory issuing the product to the patient.
‡Numbering of nucleotide (nt) is based on "A" of AUG

## Guidelines for Molecular Testing

The CBGG published ISO format guidelines for molecular testing for blood groups in 2007. The AABB standards for molecular testing for red cell, platelet, and neutrophil antigens was published in 2008.[6,7] AABB is currently assembling accreditation guidelines and training accreditors to certify laboratories that perform molecular testing for red cell, platelet, and neutrophil antigens. The intent of the CBGG is to remain as an independent forum and voice for molecular testing guidelines in ISO format for use by international laboratories. The members will update, modify, or otherwise amend the CBGG guidelines by process of discussion and consensus. The CBGG guidelines will not become standards as such to reflect the fact that the CBGG is not responsible for laboratory inspection or accreditation.

## Proficiency Program

As of spring 2008, the alleles of RBC antigens for proficiency exchanges are currently restricted to *RHCE*E/RHCE*e, GYPB*S/GYPB*s, KEL*1/KEL*2, FY*A/FY*B, FY*–67C/T GATA*, and *JK*A/JK*B*. The cost of sample preparation and shipping the DNA sample is borne in turn by each submitting laboratory. To participate in the sample exchange, proficiency program members must agree to provide a sample for distribution in a subsequent year through a predetermined rotation. Although participation in the CBGG proficiency program mandates that samples be discarded after the results have been validated, proficiency program members must ensure they comply with the requirements of regulatory bodies. Thus, before joining the proficiency exchange program and committing to supplying a sample for the exchange, new members should address their institutional requirements on informed consent. To prevent communication errors caused by different reporting mechanisms, a report form has been developed specifically for the CBGG proficiency program, a copy of which is provided in Figure 1 with examples. The proficiency evaluations for platelets and neutrophils are distributed among a group of members headed by Vagner Castro (Platelet Immunology Laboratory of Hematology and Hemotherapy Center of the State University of Campinas, UNICAMP, Campinas, São Paulo, Brazil). Serologic confirmation is not mandated by this group because of the lack of regulated antisera.

## Electronic Data Records and Databases

Members of the CBGG have recognized the need to provide manufacturers of electronic laboratory information systems (LIS) with appropriate input as they make decisions on changes to their operating systems. Presently, LIS do not have place-holder fields for genotype results or the capability to compare the DNA test result to the phenotype when available. Neither do algorithms exist to make phenotype predictions from the DNA test results. The CBGG members also discussed that a position paper from the CBGG could be developed to outline what users desire from manufacturers of DNA testing platforms and what nucleotide targets are needed to define a predicted antigen phenotype. It was recommended that a focus group be assembled to address LIS user requirements.

**CBGG Proficiency Exchange Program Result Form**

**NOTE: Report results on this Form and use the nucleotide designation from "List of Targets…. " in the current CBGG Document.**

**Date sent:** _____ **Date due:** _____

| | Originating Laboratory: | Receiving Laboratory: |
|---|---|---|
| Name: | | |
| Address: | | |
| Phone #: | | |
| Fax #: | | |

**DNA Sample ID:** _____ **Molecular Assay Requested:** [*JK*A/B* or *JK*01/02*]

**Receiving (Testing) Laboratory:** **Date sample arrived:** _____

| DNA Method | DNA Result (Genotype) | Predicted Phenotype | Technologist Date | Supervisor Date |
|---|---|---|---|---|
| [AS-PCR] | [*JK*A/JK*B*] | [Jk(a+b+)] | [Signature] | [Signature] |
| | | | [Date] | [Date] |

**Comments/Disclaimers:**

**Originating (Verification) Laboratory:**
**Acceptable response:** _____

| DNA Method | DNA Result (Genotype) | Actual Phenotype | Reviewed by: Date |
|---|---|---|---|
| [PCR-RFLP] | [*JK*A/JK*B*] | [Jk(a+b+)] | [Name] |
| | | | [Date] |

**Comments/Disclaimers:**

**Acknowledgement of verified results:** _____

Originating Laboratory: Complete all information for the receiving laboratory to perform testing.
Testing Laboratory: Fill in testing information; sign and date. Fax form to submitting laboratory.
Submitting Laboratory: Fill in results of submitting laboratory, sign and date. Fax verification to testing lab. NOTE: Discard DNA as soon as verification is received

**Fig. 1.** Example of the CBGG proficiency exchange program result form.

## Conclusions

The CBGG is a self-help, not-for-profit organization designed as an interactive collaborative for members to learn from each other and to strive to achieve excellence in molecular testing of blood group, platelet, and neutrophil antigens. Anyone interested and willing to contribute intellectually is welcome to join. Important information on analyte specific reagents in the context of laboratory-developed tests, decisions on the specifications of information systems, and the appropriate targets for molecular testing are important topics for discussion in 2010.

**Acknowledgments**

We thank Robert Ratner for help in the preparation of this manuscript. The findings and conclusions in the article should not be construed to represent any agency determination or policy.

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**Manuscripts**

The editorial staff of *Immunohematology* welcomes manuscripts pertaining to blood group serology and education for consideration for publication. We are especially interested in case reports, papers on platelet and white cell serology, scientific articles covering original investigations, and papers on new methods for use in the blood bank. Deadlines for receipt of manuscripts for consideration for the March, June, September, and December issues are the first weeks in November, February, May, and August, respectively. For instructions for scientific articles, case reports and review articles, see Instructions for Authors in every issue of *Immunohematology* or on the Web at www.redcross.org/immunohematology. Include fax and phone numbers and e-mail address with all articles and correspondence. E-mail all manuscripts to immuno@usa.redcross.org.

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